FY14/16 Chemical Biological Technologies Department – Revision #2
Questions and Answers

Topic CBA-01

Question: What is your definition of a "far-forward diagnostic and surveillance (FFDS)" device and what are the specifications of such a platform?

Answer: The definition is simple to use, low complexity medical diagnostic and detection/surveillance devices for use in the field (at the point of need) by non-certified laboratory personnel (both military and local health care clinic assistants). These tests need to function properly under austere conditions (high temperature 37C, high humidity 95%, high altitude) and in low resource settings (lacking electricity, air conditioning, good lighting, etc.). The ultimate application of science and technology towards their successful development and, ultimately, the application of such devices should lead to the generation of information to be used in the identification and diagnosis of diseases whose cause is an infectious agent or toxin; i.e. must detect the analyte (target pathogen, biomarker, and/or metabolite) at levels of sensitivity and specificity for clinically relevant levels. There are no performance specifications provided to Offerors.

Question: Where can I find the list of biological and chemical threat agents that are relevant to the program?

Answer: http://www.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/Pages/CatA.aspx

Question: Is there a focus on certain biological and/or chemical threat agents that the program is targeting?

Answer: This topic solicits for experimental "characterize and analyze the critical physicochemical properties of vertical flow" platform, not a specific target.

Question: Is there a desired degree of multiplexed identification the program is looking for (i.e. the number of threat agents to be detected simultaneously)?

Answer: Multiplexity is not specified.

Question: To characterize and analyze the critical parameters of vertical flow platform, model multiplexed immunoassays need to be used. Does the model assay need to be a biological and/or chemical threat agent detection assay?

Answer: The model needs to be biological, but a specific target is not specified.

Question: The program calls for study of "paper-based" vertical flow devices. "Paper" is traditional made from "cellulose". But vertical flow device in the cited reference used

"nitrocellulose membrane." Can you clarify what "paper" means (i.e. what kinds of materials are included)?

Answer: Whether designs are fundamentally cellulosic paper or laminates of paper in combination with modified cellulose polymer membrane or other material is entirely the responsibility of the Offeror.

Question: Do you have any specifications for performance validation of the study?

Answer: There are no performance specifications provided to Offerors.

Topic CBA-02

Question: Are blood/plasma samples the only samples that we can use? Is it possible to use other types of samples in addition to blood/plasma samples to determine bacterial vs. viral infection?

Answer: Other CLINICAL specimen types (i.e. body fluids) are possible, but must represent systemic responses rather than infections limited to specific anatomic location.

Question: Are differential immune markers specifically being sought or would evidence of bacterial or viral metabolism or replication along with immune markers also be responsive?

Answer: Immune makers are NOT specifically being targeted. The panels biomolecular makeup; however, must be amenable to being applied to a fieldable Point-of-Care device for use in field forward testing locations.

Question: Please clarify Outline Item #4 that states: "Demonstration that panel responses colonization epi-phenomenon."

Answer: The statement should read: "Demonstration that the panel responses DIFFERENTIATE INFECTION FROM colonization epi-phenomenon."

Topic CBA-03

Question: Is this topic strictly for clinical diagnostic testing or does it need to include environmental testing?

Answer: The desired outcome of the program is to have a diagnostic platform and those which are diagnostic in nature will be deemed more responsive to the solicitation; however, unique environmental systems would be considered if there was significant improvement to the current state of the art.

Question: Will DTRA coordinate the third party evaluation (topic paragraph 4) and/or should the responder include this in their SOW/budget?

Answer: DTRA will assist in the coordination and planning of the third party evaluation.

Question: Please provide an example of a toxin target that would be responsive.

Answer: Bacterial Toxins are of primary interest Staphylococcus enterotoxin type B and Botulinum toxin.

Question: Is demonstration of an 8-assay panel required, or is it acceptable to demonstrate a smaller panel (E.g. Ebola surface protein and one relevant toxin) on a device capable of performing an 8-plex assay panel?

Answer: A submission that can demonstrate the full 8-assay panel would be deemed more responsive than those that would demonstrate a smaller panel.

Topic CBA-04

- **Partnering with other/foreign organizations.**

Question: Is there a list of countries and/or types of facilities (i.e., NGO, governmental, private sector, academic, UN bodies) that DTRA is able to work with for this project?

Answer: There is no list of specified countries or types of facilities at this time. Partners able and willing to work through the performer on this effort, in support of the Biosurveillance Ecosystem (BSVE) Program, are applicable so long as they are not a prohibited source pursuant to Federal Acquisition Regulation (FAR) Part 25.7.

Question: Will international partners be limited to those countries in which DTRA/CBEP (Cooperative Biological Engagement Program) are already actively involved through other CTR (Cooperative Threat Reduction) efforts? For example, DTRA/CBEP is not currently engaged in Indonesia. Would Indonesian facilities be excluded from consideration?

Answer: International partners are not to be limited to countries in which DTRA/CBEP are engaged with. The BSVE Program is an effort funded through the Chemical and Biological Technologies Department (CB) of DTRA, separate from DTRA/CBEP. Partnering is open to countries/organizations/facilities willing and able to collaborate so long as they are not a prohibited source pursuant to FAR Part 25.7.

Question: Are there preferred international partners? (WHO, OIE, FAO, CDC, USAID, etc.) Can we partner with employees of local governments e.g., city administration, in foreign countries?

Answer: Any of the aforementioned international organizations may be candidates for collaboration partners, and the BSVE Program is open to partner with any other interested organizations willing to share information and collaborate. This includes local, state, and city-level partnerships, provided that the appropriate documentation, approvals, and/or agreements are in place to do so and they are not a prohibited source pursuant to FAR Part 25.7.

Question: Would partnering with foreign NGOs be simpler, from DTRA's point of view?

Answer: DTRA will not be directly funding any of the international partners or recipient organizations. The funding mechanism will be the responsibility of the performer as any international partner shall be proposed as a subcontractor. For efforts proposed under this program, DTRA will not vet foreign partners; however, the DTRA Contracting Officer is responsible for reviewing any subcontractor's proposal to ensure that the proposed subcontract is appropriate for the risks involved, consistent with current policy, laws and sound business judgment. As such, the Contracting Officer may require consent or approval to subcontract pursuant to FAR Part 44.

Question: Do existing MOUs address the issue of providing funding to international organizations directly from DTRA to the recipient organization?

Answer: DTRA will not be directly funding any of the international partners or recipient organizations. Funding of such partners will be the responsibility of the performer selected to conduct the DTRA funded work, and this subcontracting arrangement should be factored into the overall cost proposal.

Question: Will DTRA vet our foreign partners? What type of information would DTRA need to execute proper vetting?

Answer: For efforts proposed under this program, DTRA will not vet foreign partners, since they will be considered subcontractors. However, the DTRA Contracting Officer is responsible for reviewing any subcontractor's proposal to ensure that the proposed subcontract is appropriate for the risks involved and consistent with current policy, laws and sound business judgment. As such, the Contracting Officer may require consent or approval to subcontract pursuant to FAR Part 44.

Question: Are there any coordination requirements DTRA has in engaging with international partners, like meeting regularly with Department of State counterparts at embassy when in-country, or standing teleconferences?

Answer: There are no coordination requirements specific to engaging with international partners, for this effort. However, quarterly interim progress reviews, kickoff, closeout meetings will be necessary for any project funded through the BSVE Program. Foreign partner engagement in such meetings may be of benefit, depending on the needs and scope of the proposed effort.

- **Funding mechanism for partners.**

Question: What mechanism is in place to transfer funding from a funded project to partnered organizations/entities? Is this a contract that the primary grant awardee would address, or does DTRA distribute the funds?

Answer: DTRA will not distribute the funds to partnered organizations/entities. The funding mechanism for this will be the responsibility of the Offeror. The foreign partner would be considered a subcontractor for the effort.

Question: Can that funding be provided to international institutions, be they governmental, public university, private, NGO, etc.? Please describe that mechanism so that we may brief our partners on it.

Answer: Please refer to the response above.

Question: Partnering would require us to fund our partners. Can DTRA send funds to local governments in foreign countries (we realize that some local governments in foreign countries may not be able to accept US funds).

Answer: Please refer to the response above.

- **Data contributed by foreign partners**

Question: We expect that our foreign partners may contribute data into an application some of which they may share openly, and some that they may wish to keep to keep private e.g., in an extreme case, the data may be CFGI-MOD (confidential foreign government information, modified handling authorized). Is such a dichotomy allowed, or should the data be such that it is openly sharable with all BSVE users?

Answer: Data ingested into the BSVE through applications should not contain any personally identifiable information (PII). Additionally, it is not envisioned that any confidential information will be ingested at this point in time; openly shareable, de-identified data is preferred.

Question: Once a foreign partner contributes data to an app, do they still own their data? Can they, for example, delete their contributions after 6 months?

Answer: The system is designed to share data, and DTRA is seeking partners willing to openly contribute information. We are currently not seeking any owned data or software/applications that will require licensing.

Question: If DTRA funds an app, we understand that they own rights to it. However, are we allowed to use the same app to obtain further funding from other sources, commercialize it and use it in technology transfers? We are trying to find a way of making the effort self-sustaining.

Answer: Yes, this supports the BSVE paradigm of sustainability; the offer can use the same app to obtain funding from other sources, and commercialize it.

Topic CBA-05

Question: Are you interested in wearable chemical sensors (without biological capabilities)?

Answer: The intent of the topic is to determine an early onset host response to a threat. While sensors that detect chemicals is of interest to DoD, for the purpose of this topic, a sensor which

can detect an early exposure to Chemical and Biological threats through host response, is deemed more appropriate.

Question: Our current targets are CWAs and high risk TICs, is this appropriate for the proposal?

Answer: The intent of the topic is to determine an early onset host response to a threat. While it may be appropriate to detect threat agents themselves, it is more appropriate to detect the host response to exposure than the threat.

Question: Can you elaborate on extended mission lifetime (i.e. 8 hours, 24 hours, weeks, or months)?

Answer: The intent of the topic is to find 'wear and forget' sensors for exposure to CB threats. The goal is to produce sensors that would be analogous to or better than commercial performance health monitoring or patch based heath sensors. In such a form factor, multiday or longer use should be expected.

Topic CBM-02

Question: Can Targets B and C be specified by Offeror?

Answer: Targets B and C can be specified by the Offeror.

Question: Is Staphylococcus enterotoxin B (SEB) an obligatory target or can it be substituted with another toxin target e.g. anthrax?

Answer: SEB is not an obligatory target; however, proposals that include efforts to develop vaccines against SEB will be the highest priority.

Question: Is it obligatory to have each a viral, a bacterial and a toxin (SEB) target included in the application? Could Offeror substitute the bacterial agent with a viral target?

Answer: While targets B and C can be specified by the Offeror, the following pathogens will be high priorities for the program: Tularemia, Q Fever, and western/eastern/Venezuelan equine encephalitis. The WEEV/EEEV/VEEV target would be a trivalent formulation to protect against all three.

Topic CBM-04

Question: What range of targets would be acceptable?

Answer: The Offeror will demonstrate utility of the platform prophylaxis technology to target a priority weaponizable biologic. Proposals that maintain focus to optimize platform performance are preferred; however, if the Offeror opts to assess broader utility in the later years of the proposal, utility demonstration of the platform technology against at least one bacterial, viral and toxin targets is a preferred approach. Specific targets could include, but are not limited to:

Filovirus (Excluding full-length GP), Chikungunya virus, Francisella tularensis, Bacillus anthracis (excluding Protective Antigen and Lethal Factor), Burkholderia mallei and pseudomallei, Staphylococcal Enterotoxin B (SEB).

Targets could be native structures or genetically modified proteins with enhance immunogenicity and/or immunodominance patterns.

Question: Could we use F. tularensis or Burkholderia spp. as potential bacterial targets for this work?

Answer: Yes.

Question: What are the other targets - target b and c?

Answer: High priority targets for B and C will be Tularemia, Q Fever, and western/eastern/Venezuelan equine encephalitis.

Topic CBM-06

Question: Please define and explain the "Target Product Profile that will be required in Phase II".

Answer: Target Product Profile is a strategic tool to describe the current state, and the desired end state of a product. Generally, you would see desired metrics such as formulation, route of delivery, dosing regimen, toxicity, storage stability, and more. The parameters defined are somewhat contingent on the current maturity of a product; it can be difficult to devise a concrete TPP in the discovery phase. However, a TPP may be revised throughout development and a successful product development program would be expected to have a general idea of the goals it is trying to achieve, in the context of pharmaceutical development.

Question: It states that “Basic research studies focusing on ... structural analysis of antibacterial targets” is NOT of interest. We would like to use structural and computational methods to better design compounds by seeing what contacts can be optimized between the compound and its target. This improves potency. Can structural and/or computational studies be included as a means to design better compounds, not as basic research but as part of the lead optimization portion of drug development?

Answer: While the passage quoted is accurate - studies related to structural characterization of novel targets are not responsive, as demonstrated by the priorities for "Stage of Development, 2a. Lead validation and optimization," rational drug optimization, including that directed by SAR, is considered responsive.

Topic CBS-01

Question: Discovery of New Central Nervous System (CNS) Accessible Acetylcholinesterase Reactivators. The final sentence of the topic description states that oxime-based reactivators will not be considered. What is the rationale behind this choice, given that so far the oxime-(like) functionality has always been shown to be the nucleophile of choice compared to other nucleophiles in the generally accepted mechanism of AChE reactivation which involves a nucleophilic attack on the phosphonate residue? What are the specific objections to the use of oxime-functionalities in future reactivators?

Answer: The current effort seeks to identify new enzyme reactivators without oxime functionality in an effort to diversify the medical countermeasure portfolio and reduce risk.

Question: Should the preliminary literature search involve open source literature and classified literature?

Answer: Literature search can include both literature types. However, it is not necessary as this is a basic scoping study to determine impact of microbe preparation on viability prior to and post aerosolized state to help inform future experiments.

Question: Does DTRA want proposals to determine the effects of media and sample preparation on viability in the aerosolized state only? Or, does DTRA also want to include determining the influence of environmentally factors on particles after having settled out of the aerosol and onto different types of surfaces?

Answer: DTRA wants proposals to determine the effects of media and sample preparation on viability in the aerosolized state. DTRA is looking to fill a gap in current knowledge (primarily concerning gram negative bacteria and viruses that are impacted by the preparation technique) to help better inform future experiments.

Question: Does DTRA have a preference to using BSL-1, BSL-2 , or BSL-3 microorganisms or for specific microorganisms or surrogates?

Answer: There is no preference on microorganisms. DTRA requests that this study select a microbe that is "less evolutionarily dynamic" or rather a bacteria with a low mutation rate and BSL-1 or 2 surrogate bacteria for those of interest should be adequate. Gram negative bacteria are more impacted by preparation technique and would help fill the knowledge gap.

Question: Can you define the term "less evolutionarily dynamic"?

Answer: Please refer to the response above.

Topic CBS-04

Question: This question pertains to Topic CBS-04, Media Scoping Study, beginning on page 22 of the BAA Amendment 10. It appears that the “Objective: Develop/refine standardized

methodologies for biological aerosol research" and "Impact" text, though found as part of CBS-03, should actually be part of Topic CBS-04. Is this assumption correct?

Answer: Yes, impact and objective should be part of Topic CBS-04.

Topic CBT-01

Question: Does research under this topic include antibody technologies to support efficient, rugged, and inexpensive functional molecular and cellular systems for effective physical and medical countermeasures against Chemical/Biological warfare agents (CBWA)?

Answer: No.